

AMENDMENTS TO THE SPECIFICATION

Please amend the specification as follows:

[0005] The authors have also shown that fusion proteins between the Gb3 receptor-binding non toxic B-fragment of bacterial Shiga toxin derived from *Shigella dysenteriae dysenteriae* and an antigen, or an epitope from a model tumor antigen, can elicit specific cytotoxic T lymphocytes response (CTL), whereas each moiety of said fusion protein does not lead individually to CTL induction (1,2, and WO 99/03881).

Please amend paragraph [0056] as follows: [0056] ~~primer A': "5'-GACTACTACGTTTTTAMC-3'~~ primer A': primer ShigaAtpE "5'-CACTACTACGTTTAAAC-3' (SEQ ID no 5), and,

Please amend paragraph [0068] as follows:

[0068] The present invention also provides a method for delivering a sequence of interest into the ~~MITG~~ MHC class I pathway using a product obtained by covalent binding of the Cys moiety of the universal carrier with said sequence of interest; this method is advantageous to elicit a CTL ~~respons~~ response to a given antigen or epitope thereof as far as the product is specific to the cell involved in the MHC class I pathway.

Please amend paragraph [0081] as follows:

[0081] ~~FIG. 2a~~ represents ~~the~~ the coupling of Type2 of Pep2 [as defined in example 2] to STxB-Cys, followed by an in vitro antigen presentation assay on D1 dendritic cells, as described in (2). Two different preparations of STxB-Cys coupled to the SL8 peptide, an immunodominant epitope of ovalbumin were used (termed 4A and 9A). Upon fixation, antigen presentation is abolished showing that no extracellular processing occurred.

[0089] ~~FIG. 9~~ shows MHC class ~~I~~ I and ~~II~~ II restricted antigen presentation induced by incubation of D1 cells with STxB-Cys-Ova. See text for details.

Please amend paragraph [0091] as follows:

[0091] In a preferred embodiment, the plasmid pSU108 (7) was modified to introduce the Cysteine codon tgt at the 3' end of the B-fragment cDNA. PCR

primer A: SEQ ID no 3 (5'-

~~AGCGAGTTATTTTCGTTGTTGACTCAGAATAGCTC-3')~~ (5'-

AGCGAAGTTATTTTCGTTGTTGACTCAGAATAGCTC-3') and primer A': SEQ

ID no 4 (5'-~~GAGCTATTCTGAGTCAACACGAAAAATAGCTC-3')~~ (5'-

GAGCTATTCTGAGTCAACACGAAAAATAACTTC-3') were used with plasmid

specific primers ShigaAtpE: SEQ ID no 5 (5'-~~CACTACTACGTTTTTC-3')~~ (5'-

CACTACTACGTTTTAAC-3') and Shiga-fd: SEQ ID no 6 (5'-

CGGCGCAACTATCGG-3') to produce DNA fragments which, in a second PCR with

primers Shiga AtpE and Shiga-fd yielded a fragment that was cloned into the

SphI and SalI restriction sites of pSU108. Sequences derived by PCR were

verified by dideoxy-sequencing.

Please amend paragraph [0139] as follows:

[0139] Our preliminary evidence suggests that chicken ovalbumin can be coupled to STxB-Cys. These experiments have ~~be-n~~ been done with the SPDP heterobifunctional cross-linker. (Carlsson et al., 1978).

Please amend paragraph [0148] as follows:

[0148] 0.5 μ M of STxB-Cys-Ova was incubated with HeLa cells on ice. The cells were washed and shifted to 37° C. for 45 min, fixed, and stained for the indicated antibodies. As shown in FIG. 8, when STxB-Cys and Ova were linked by MBS, Ova immunoreactivity could be detected together with STxB immunoreactivity in the Golgi apparatus, stained by Rab6. When both proteins are incubated as separate ~~ntities~~ entities with HeLa cells, only STxB-Cys is transported to the Golgi, while Ova cannot be detected on the cells. These data clearly show that couples STxB-Cys is still transported in the same manner as uncoupled STxB-Cys, and that Ova is vectorized via STxB-Cys.

Please amend paragraph [150] as follows:

[0150] In a second experiment, we have pulsed the same D1 dendritic H2^b restricted cell line with either Ova alone or with STxB-Cys-Ova. No presentation of the Ova-derived immunodominant SL8 peptide (Ova₂₅₇₋₂₆₄) was observed when the D1 cells were sensitized with up to 100nM of free Ova, while 1-10 nM of STxB-Cys-Ova allowed the presentation of the SL8 peptide, as revealed by the specific B3Z hybridoma that ~~recognize~~ recognize the SL8 peptide in the context of K^b molecules. As a control, it was shown that no activation of an irrelevant hybridoma was observed under the same experimental conditions.